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Viral load in children with congenital cytomegalovirus infection identified on newborn hearing screening

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ABSTRACT

Background: Congenital cytomegalovirus (CMV) infection is the most common non-genetic cause of sensorineural hearing loss (SNHL) in children. However, congenital SNHL without other clinical abnormalities is rarely diagnosed as CMV-related in early infancy.
Objectives: The aim of this study was to identify and treat patients with congenital CMV-related SNHL or CMV-related clinical abnormalities other than SNHL. The association between CMV load and SNHL was also evaluated.
Study design: Newborns who had abnormal hearing screening results or other clinical abnormalities were screened for congenital CMV infection by PCR of saliva or urine specimens, and identified infected patients were treated with valganciclovir (VGCV) for 6 weeks. The CMV load of patients with or without SNHL was compared at regular intervals during as well as after VGCV treatment.
Results: Of 127 infants with abnormal hearing screening results, and 31 infants with other clinical abnormalities, CMV infection was identified in 6 and 3 infants, respectively. After VGCV treatment, 1 case had improved hearing but the other 5 SNHL cases had little or no improvement. Among these 9 patients with or without SNHL at 1 year of age, there was no significant difference in CMV blood or urine load at diagnosis, but both were significantly higher in patients with SNHL during VGCV treatment.
Conclusions: Selective CMV screening of newborns having an abnormal hearing screening result would be a reasonable strategy for identification of symptomatic congenital CMV infection. Prolonged detection of CMV in blood could be a risk factor for SNHL.

1. Background

In developed countries, congenital cytomegalovirus (CMV) infection occurs in 0.2–2.0% of births and is one of the most frequently identified members of the TORCH complex [1,2]. Because most infants congenitally infected with CMV are considered to be asymptomatic at birth, the number of these patients is underestimated [2]. Sensorineural hearing loss (SNHL) is the most common sequela, and abnormal findings on ultrasonography and brain magnetic resonance imaging are associated with SNHL [3]. This disease is the most common non-genetic cause of SNHL in children [4]. In Japan, 12–15% of cases with severe SNHL were associated with congenital CMV infection [5]. Because congenital CMV infection is a potentially treatable cause of SNHL, early identification is important.

However, congenital SNHL without other clinical abnormalities is rarely recognized to be CMV-related in early infancy. Generally, it is recommended that neonates who do not pass hearing screening receive a comprehensive audiological evaluation no later than 3 months of age [6]. Infants with SNHL are suspected to have congenital CMV infection, but it is often too late to distinguish perinatal from congenital infection, or to offer antiviral treatment. Universal newborn screening for congenital CMV infection could allow for early identification and intervention. There is fair evidence of a potential benefit from antiviral treatment during the neonatal period and early infancy for children with congenital CMV-related SNHL [7]. On the other hand, potential harm arising from universal

Abbreviations: CMV, cytomegalovirus; SNHL, sensorineural hearing loss; VGCV, valganciclovir; MRI, magnetic resonance imaging; AABR, automated auditory brainstem response; OAE, oto-acoustic emission; US, ultrasound; SGA, small for gestational age; WM, white matter.

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Table 1
Summary of 9 patients with congenital CMV infection.

Case	Initial identification	Gestational age (weeks)	Weight at birth (g)	CMV load in blood[a] (copies/mL)	CMV load in urine[a] (copies/mL)	Cerebral MRI findings	Delayed development at 1 year of age[b]	Hearing function at 1 year of age
1	OAE	39	2592	1.8×10^4	3.2×10^7	WM abnormality	Yes	Profound bilateral SNHL
2	OAE	38	2810	Undetected	5.8×10^3	VentriculomegalyWM abnormality	Yes	Profound bilateral SNHL
3	AABR	39	2590	2.4×10^2	2.4×10^7	VentriculomegalyWM abnormality	No	Severe bilateral SNHL
4	AABR	37	2230	1.1×10^4	9.5×10^7	WM abnormality	Yes	Moderate bilateral SNHL
5	AABR	39	3366	1.3×10^3	1.3×10^3	Normal	No	Profound bilateral SNHL
6	AABR	41	3440	Undetected	3.1×10^2	Normal	No	Normal
7	Cerebral US	36	2400	4.2×10^3	3.0×10^2	Subependymal cyst	No	Normal
8	Cerebral US	35	2002	9.8×10^3	6.8×10^6	Subependymal cyst	No	Normal
9	SGA	38	2310	7.2×10^2	6.7×10^5	Normal	No	Normal

CMV, cytomegalovirus; MRI, magnetic resonance imaging; OAE, oto-acoustic emission; AABR, automated auditory brainstem response; US, ultrasound; SGA, small for gestational age; WM, white matter; SNHL, sensorineural hearing loss.

[a] CMV loads at diagnosis are shown.

[b] An adaptive developmental quotient (DQ) was obtained from the ratio of the child's developmental age to the chronological age multiplied by 100. Developmental delay was defined as <70 of the DQ.